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## AN UNUSUAL CASE OF NOCARDIOSIS

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This case is considered worthy of record for several reasons:

1. The patient was a physician and, as in this case, physicians often fail to receive as good attention as other patients. Too much is taken for granted by the physician himself, while the view of the rest of the world is: "Physician, heal Thyself."
2. The diagnosis was completely missed during life.
3. Necropsy with bacteriologic and pathologic study cleared up the whole condition.
4. The infection is a rare one.

The physician was 53 years of age and owned and managed a sanatorium for mental and nervous diseases near a large Eastern city. He had always enjoyed unusually good health up to two years ago. He was a tall, thin man of English type. His family history and previous history are uninformative except that one sister had a mild attack of tuberculosis several years ago from which she has recovered.

**Present Illness.**—In October, 1919, the patient, while eating soup inhaled what he thought was a small piece of bone. It seemed to lodge in the right side of the chest. A nurse who was present said, after the death of the patient, that he nearly suffocated at the time of the accident. The patient, however, minimized the accident and cautioned the nurse to say nothing about it to his family. Shortly afterward, a physician on a nonprofessional visit observed that he apparently had a "bad cold" and was coughing considerably. He made light of the trouble, and though it was suggested that he have a bronchoscopic examination, he did not consider it necessary, saying that he thought that if he had inhaled the bone it was only a small splinter. During the following months he complained of pain in the right side and coughed a good deal. In February, 1920, he had a severe attack of influenza, with high temperature and some pneumonia. The trouble was especially marked on the right side and was accompanied by pain on breathing and a good deal of expectoration. Cultures of sputum at this time showed *Staphylococcus aureus* and *Micrococcus catarrhalis*; the leukocyte count was 15,900. After partial recovery he was given a thorough examination. Roentgen-ray plates were negative, especial search being made for the bone; examination of the sputum proved negative for tubercle bacilli; guinea-pig inoculations were inconclusive because of the early death of three animals from complicating infections. Another specimen of sputum was requested but was not received. The Wassermann reaction was negative; blood sugar 0.11%; urea nitrogen 13.7 mg. It was concluded at this time that the case was one of postinfluenzal bronchitis or bronchiectasis. The teeth were examined with the roentgen ray, and several teeth with apical abscesses were extracted. The patient improved a great deal during the summer and the following fall of 1920 seemed to be active and well. In February, 1921 he had another attack—influenzal in character—and became considerably run down in weight and vitality. In May, 1921, he went to Atlantic City for recuperation, but felt so bad that he returned

after about two weeks. He had a slight fever at this time, shortness of breath, pain in the right side and coughed a good deal. He was seen at this time by a nose and throat specialist and a lung specialist, and they found evidences of what was thought to be a latent tuberculosis in both apexes with a somewhat more active lesion in the lower part of the right lung. A roentgenogram showed a slight lesion in the latter location. It was recommended that the patient go to a northern sanatorium for rest and treatment for tuberculosis. Sputum examinations at this time were negative for tubercle bacilli; some nonacid-fast rods were seen but no importance was attached to them. During July and September, 1921, the patient was in the north, where physicians thought he showed slight tuberculous lesions of both apexes, especially the right. The sputum was negative for tubercle bacilli. He improved considerably in weight, walked and drove about a good deal and was preparing to return when, on Sept. 7, he had an attack of mental confusion and developed a slight general paralysis. This passed off in a day or two, but he had a red nodule on one wrist, and an old buckshot wound on the right leg became somewhat inflamed. He was making further plans to return home when, on Sept. 9, he had a convulsive attack accompanied by unconsciousness, a wrist drop of the right hand appearing after the first convulsion. The blood examination showed: leukocytes 25,200; polymorphonuclears 78%. The next day he was mentally clear but weak. A spinal puncture on the 11th showed an increase in globulin, cells 4, polymorphonuclears 13%, lymphocytes 84%. On that day there was another attack of confusion followed by convulsion, after which the entire right side was paralyzed. The urine showed a trace of albumin, a few casts and some red blood cells. Blood cultures were made which were sterile at the end of a week. Blood count: leukocytes 24,000; polymorphonuclears 85%. The temperature was elevated very little. A probable diagnosis of cerebral hemorrhage or embolism was made. The patient was taken home barely alive on Sept. 11 and died on the 15th. A consultant at his home made a probable diagnosis of thrombosis. Another leukocyte count was requested, but the patient died before it could be made. He never became fully conscious. During the last few days his left side also showed some paralysis.

#### EXTRACTS FROM THE NECROPSY REPORT

The body was that of a well developed, somewhat emaciated white man. Panniculus moderate in amount but contains little fat.

*Brain.*—The dura is adherent to the brain along the superior longitudinal sinus where the pachionian bodies seem to be increased in size. All vessels are markedly injected, and there is some exudate about the vessels in the posterior portion of the left cerebrum which bulges posteriorly. There is considerable edema of the membranes. On section, two abscesses were found, the larger in the left cerebrum being 9 cm. in length from before backward, and about 5 cm. in diameter, occupying the greater part of the middle of this lobe. In the right lobe was a similar abscess about 5 cm. in diameter, more or less spherical in shape. The abscesses have a ragged wall, not clearly outlined, and the centers contain fluid pus. The right ventricle contains a cloudy fluid, while the left is clear. The abscesses compress the periphery and both involve the internal capsule.

*Thorax.*—Left pleural cavity is moist, and there is one fibrous adhesion at the apex. Elsewhere the lung is free, the visceral pleura being somewhat duller than the parietal.

Right pleura shows a few firm adhesions at the apex and a free portion from about the lower margin of the second rib to the upper margin of the

fourth rib in the midaxillary line. From there, to and including the base, the lung is adherent by large delicate fibrous adhesions, the interstices between the adhesions being filled with a gelatinous exudate.

*Lung.*—The left lung shows the pleura at the apex markedly thickened by elevated opaque, yellowish white, firm, coalescing nodules, the area covered by this thickening being approximately 2.5 cm. anteroposteriorly and 5 cm. from within outward. The thickening extends only a few millimeters into the lung-parenchyma, and while there are a few small points of yellowish opacity between these raised nodules, there is no marked activity. The rest of the upper lobe is air-containing, and, although somewhat congested, appears relatively normal. The lower lobe shows scattered areas of thickening, the centers of which are apparently about smaller bronchi and therefore occupy the centers of the lobules. The color of the lung is a deep red with a lighter, brighter red with a yellowish tint as the color of these consolidated areas.

The right lung shows a similar condition at the apex except that its extent is 3.5 to 4 cm., maximum anteroposterior measurement, and 12 cm. maximum measurement from within outward. The area, therefore, forms a cap over the apical portion of the lung. The maximum extension of the thickening into the parenchyma of the lung is 1 cm., and there is a yellowish caseous looking area where the thickening joins the air-containing tissue. Below this area the tissue for a distance of 2 to 3 cm. appears relatively normal. It then becomes a darker red and indurated. In about the mid-portion of this lobe is a yellowish white opaque area approximately 2 cm. in diameter, the center of which, about 1.3 cm. in diameter, is soft and composed of a cheesy-like material, of a granular consistency. From this area to the hilus of the lung the nearest bronchus is surrounded by an indurated thickened area, and the wall of the bronchus itself is markedly thickened and lined by a dirty brownish red membrane covered with an exudate of similar color. The interlobar fissure has been obliterated by adhesions. At about the midaxillary line, the tissue of the upper lobe just above the interlobar separation presents an indurated mass about 3 cm. in diameter, in the center of which is a cavity about 1.5 cm. in greatest diameter lined by a dark brownish red membrane. The cavity appears to be vacant except for a small amount of dirty reddish exudate on the surface of the lining. In the upper portion of the lower lobe extending outward from the main bronchus of this lobe about 4 cm. from its origin, is an indurated mass which extends into the lung for a distance of about 5 cm. This consists of indurated dark red tissue in the periphery with a slaty reddish zone of connective tissue forming a center with soft, small abscesses averaging 3 mm. scattered through it. This right inferior bronchus shows a markedly thickened wall which is irregularly dilated surrounding a cervical vertebra of a chicken which had lodged 2.5 cm. from the origin of the right inferior bronchus. It was situated with its inferior or ventral aspect posteriorly and had lost its two inferior prolongations. The rest of the lower lobe shows an occasional bronchopneumonic patch like those described in the left lung, while the pleura over the entire lung is thickened, particularly where covered by adhesions, as described in the foregoing.

The tracheobronchial glands are relatively small in the upper areas. The large gland below the primary bronchus of the right lung has enlarged to a size of 1.5 cm. in thickness and 3 cm. in length. On section it is mottled a rather deep red and an opaque yellowish red. The upper series of glands show a few hardened foci but no evidence of tuberculous activity.

*Kidneys.*—These show cloudy swellings and are rather opaque, but the capsule strips normally. In one section near the lower pole of the right kidney is an opaque yellowish area about 2.5 mm. in diameter.

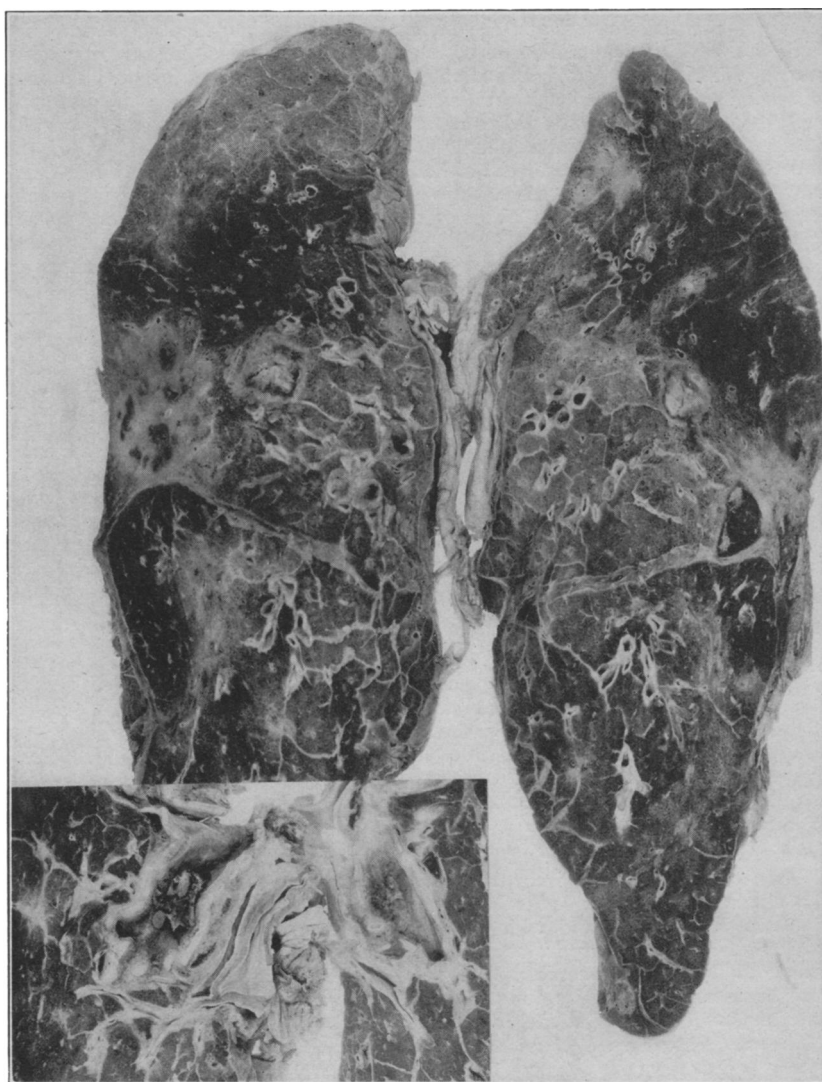


Fig. 1.—Sections of right lung showing lesions caused by *Nocardia*. Insert: Chicken vertebra in right bronchus.

## BACTERIOLOGIC FINDINGS

Bacteriologic studies were made by Major H. J. Nichols, M. C., U. S. A. At necropsy, smears were made from the pus of the largest abscess of the brain. These showed no tubercle bacilli, but a number of clusters of short, threadlike gram-positive organisms, which were diagnosed as *Streptothrix* (*Nocardia*). Several slants of infusion agar were inoculated with the pus at the time of necropsy. These remained sterile except for a slight growth of *Streptothrix* in one tube which could not be transferred to other slants. Pus from the abscess was collected in a sterile tube, and on return to the laboratory was inoculated into several deep glucose agar tubes. After a week's incubation one tube showed three distinct colonies made up of threadlike organisms similar to those found in the abscesses. These colonies have a characteristic trilobular appearance (fig. 2). The organism was in pure culture and has been transferred a number of times in deep agar, and grows freely after several days' incubation. It is a strictly anaerobic, gram-positive, pleomorphic bacillus. It stains unevenly both by Gram stain and with Loeffler's methylene blue. Branching forms are seen in the tissues; in culture no definite branching forms were seen. It was evidently in pure culture in the abscess.

*Animal Inoculations.*—A guinea-pig, inoculated subcutaneously with the pus, developed a small abscess lasting for two weeks, which showed a mixed growth of numerous threadlike organisms and staphylococci. A guinea-pig inoculated subcutaneously with the culture developed a small nodule which disappeared after about a week without breaking down. Further inoculations were made as follows: One guinea-pig was inoculated intraperitoneally with culture, one rabbit intravenously, one monkey intratracheally, and one monkey intracerebrally with culture. None of these animals showed any evidence of infection in two months. Necropsies were performed on all, and none was infected.

The organism which appears to have been the cause of the disease belongs to the anaerobic group of *Streptothrix* but is a somewhat unusual type. When injected in the pus from human lesions, it was only slightly pathogenic for guinea-pigs and lost its virulence rapidly in culture. A guinea-pig which was inoculated intraperitoneally with the pus, showed two weeks later, after a subcutaneous inoculation, an anaphylactic reaction of redness and induration about the inoculation site.

## HISTOLOGIC EXAMINATION

*Brain.*—Sections from the brain show an abscess, the contents of which are composed of polymorphonuclear leukocytes with numerous colonies of *Streptothrix* (*Nocardia*) scattered throughout the pus. The wall is composed of brain tissue over a considerable area, though in places there is thickening of the glia forming a delicate margin of gliosis. The leukocytes have infiltrated the tissue to a greater extent where this protective wall has not been formed. Blood vessels in the vicinity of the abscess show escape of leukocytes, both polymorphonuclear and lymphocytes, and brain tissue for considerable distance around these abscesses shows similar leukocytic infiltration, lymphocytes gradually predominating at a distance from the abscess wall. The meninges show some thickening in the sulci, and deep between the convolutions or lobules there is considerable exudation, particularly where the abscess approaches the surface. This exudate is composed of fibrin with rather numerous leukocytes largely of the polymorphonuclear variety. The pia is somewhat thickened over the surface of the brain which overlies the abscess. The process has destroyed brain tissue and surrounding it ganglion cells show advanced degenerative changes and there is considerable edema throughout.

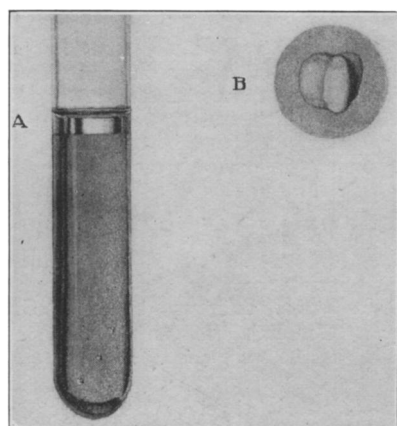


Fig. 2.—*A*, anaerobic culture from brain abscess; *B*, enlarged colony.

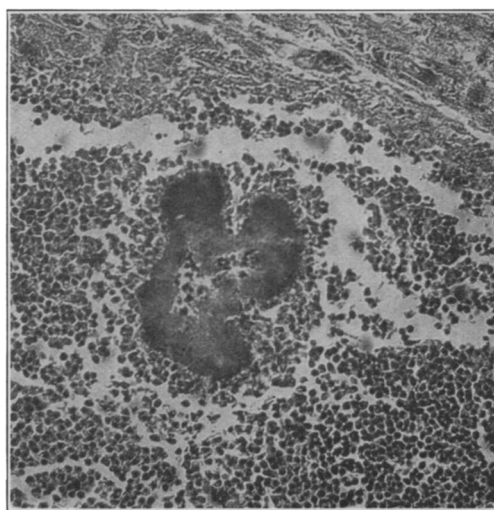


Fig. 3.—*Nocardia* in brain abscess;  $\times 100$ .

*Right Lung.*—Sections taken from the bronchus in the vicinity of the chicken bone show an intense hyperemia and denudation of the bronchial mucosa with formation of granulation tissue from the submucosa. The bronchial glands are swollen and dilated with secretion, their walls infiltrated with leukocytes, and there is an increase in connective tissue extending down from the granulating layer on the surface to the cartilages and involving to a considerable degree connective tissue between the cartilages and beneath them. Lymph nodes are hyperactive as indicated by marked increase of epithelioid cells in the nodal centers. Bacterial stains show various types of organisms, both cocci and bacilli. There are no colonies of *Streptothrix* in these areas.

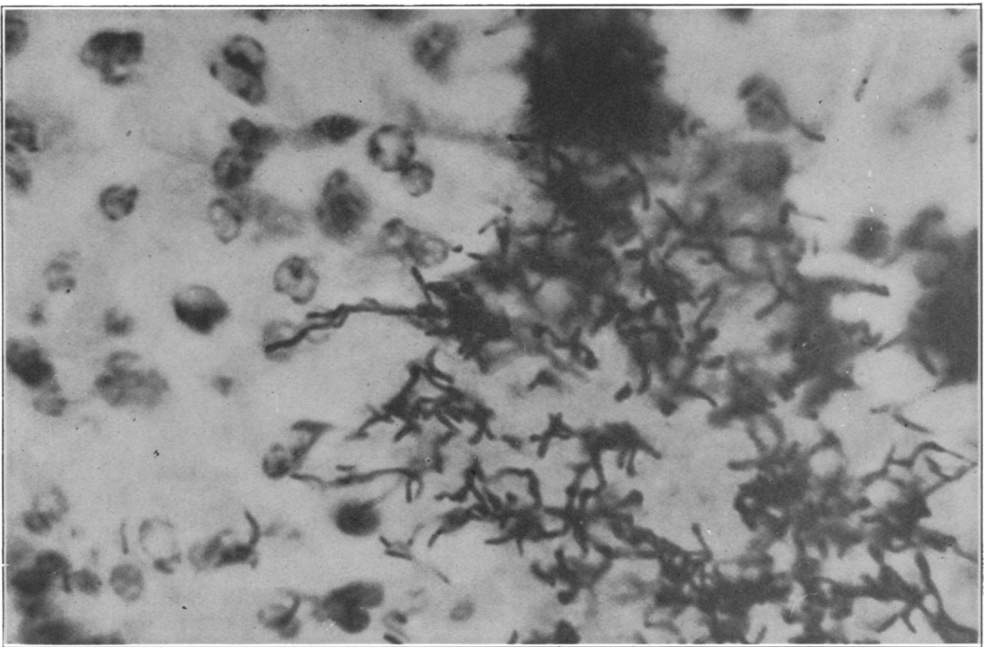


Fig. 4.—*Nocardia* in tissue;  $\times 1,000$ .

Sections from the pearly masses of the apexes show fibrosis and connective tissue which in places has become hyaline. Scattered here and there are small lymph nodes containing anthracotic pigment surrounded by a smaller zone of some younger fibroblasts than are present in the rest of the tissue. The lymph nodes are more abundant just beneath the endothelial surface. This fibrosis appears to extend only a short distance into the lung.

A section taken from one firm nodule surrounding the bronchus of the right upper lobe shows bronchial mucosa partially desquamated; the walls are thickened and the surrounding blood vessels are engorged. The surrounding air cells show a marked thickening of the alveolar walls and an atelectatic condition. The epithelium of the alveoli have for the most part become cuboidal in character. This probably represents a blocking off of this small section of the lung by reason of inflammatory changes in the bronchus.



Sections from the bluish area at the junction of the upper and lower lobes of the right lung show an advanced fibrosis of the alveolar walls resulting in an organizing process compressing the alveoli which contain desquamated epithelial cells. There is no tendency in this area for the alveolar epithelium to become cuboidal but rather to degenerate. In the outer layers there is considerable hyalin change where alveolar structure has been eradicated by the overgrowth of connective tissue. In sections nearer the abscesses in the indurated tissue the early stages of these processes are seen and vary from thickening of the alveolar wall by edema and lymphocytic infiltration to the fibrosis of the older areas. All of this tissue contains numerous lymphocytes and quite a few polymorphonuclears.

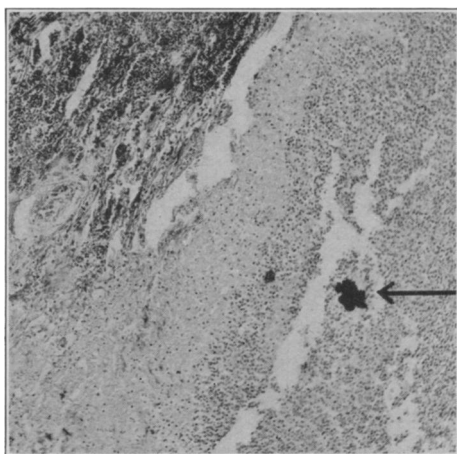


Fig. 5.—Nocardia in lung abscess.

Sections from the bronchus of the upper lobe of the right lung taken about 4 cm. from its origin show a marked thickening of the wall due to connective tissue increase in the submucosa which has surrounded and partially obliterated the glands. Gram-positive organisms, both cocci and bacilli and gram-negative bacilli, are found in the bronchi and to some extent in occasional alveoli where the exudate consists largely of leukocytes. The abscesses of the lung where filled with leukocytes show numerous colonies of *Streptothrix* or *Nocardia* (fig. 5).

*Left Lung.*—Sections taken from the bronchopneumonic areas show numerous small patches 3 or 4 mm. in diameter where the alveoli are partially filled with polymorphonuclear leukocytes. The bronchial epithelium is desquamated. The bronchi contain considerable pus. The walls of the alveoli are not markedly thickened though the blood vessels are filled with blood. There is some tendency in portions to proliferation of connective tissue cells. In addition to the leukocytes, the alveoli contain blood cells and a moderate amount of fibrin. The organisms present are a mixture of gram-positive and negative cocci and bacilli. There are no colonies of *Streptothrix* in this lung.

*Kidney.*—Glomeruli show some proliferation of the capillary endothelium and a slight degree of hydropic change. The cells of the convoluted tubules are swollen and granular. One section of the right kidney shows two small

abscesses surrounded by connective tissue thickening of considerable extent with leukocytic infiltration and vascular hyperemia throughout the thickened tissue. The abscesses contain colonies of *Streptothrix*.

*Skin*.—A section from the skin shows an infiltrating abscess in the deeper layers of the subcutaneous tissue with a slight degree of fibrosis. The abscess contains colonies of *Streptothrix*.

*Anatomic Diagnosis*.—Nocardiosis of the right lung with metastatic abscess in the brain, kidney and skin; tuberculosis of apical pleura, both lungs; bilateral bronchopneumonia; degeneration (toxic) of kidneys and liver; foreign body (chicken neck vertebra) in right inferior bronchus with secondary bronchitis and bronchiectasis.

#### GENERAL SUMMARY

The patient, two years before death, inhaled into his right bronchus a chicken vertebra. He minimized the importance of the size of the bone and repeated roentgen-ray examinations failed to reveal it. A few months after the accident the patient had a severe attack of "influenza" with pneumonia, which was especially localized on the right side. A year later there was a train of symptoms of the same character. During the interim the patient was in comparatively good health. Following this second attack until his death (a period of seven months) the patient gradually failed. He had a cough, high temperature, pain in the right side and shortness of breath. Bacteriologic examinations were negative but physical examination and roentgenograms indicated a tuberculous process. Two weeks before death there was evidence of embolic processes as indicated by the cerebral attack and the abscess on the leg. Signs were found of old tuberculosis of the apexes.

It is impossible to determine accurately the exact onset of the infection with *Nocardia*. From the clinical history it would appear that if this infection occurred prior to the second influenzal attack in February, 1921, it must at least have remained well localized, as no generalized symptoms occurred. It seems not unreasonable to suppose that the focus of diminished resistance produced by the bone in the bronchus gave a satisfactory lodging place for this organism, which probably came from the mouth and that it slowly developed during the last seven months of the patient's life, then by its formation of abscesses it gained access to the blood stream and produced a nocardial pyemia during the last two weeks. The general age of the lesions in the lung and brain indicates that this is the probable story.

The organism belongs to the *Streptothrix* group and is a rather unusual type in that it is apparently an absolute anaerobe. Such organisms have been described, but no attempt is made at this time to review the literature on infections with this type of organism.